

09/914684

JC14 Rec'd PCT/PTO 30 AUG 2001

<b>TRANSMITTAL FOR ENTRY OF PCT APPLICATION IN U.S. NATIONAL STAGE UNDER 35 U.S.C. § 371</b>	Docket No.: <b>P-LX 4948</b>
Proposed Preliminary Classification: (optional)	Class: <b>436</b> Subclass: <b>169</b>

Address to: COMMISSIONER FOR PATENTS  
Box PCT  
Attn: DO/US  
Washington, D.C. 20231

CERTIFICATE OF MAILING BY "EXPRESS MAIL"

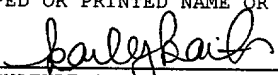
"EXPRESS MAIL" MAILING LABEL NUMBER: EL 856 979 925 US

DATE OF DEPOSIT: August 30, 2001

I HEREBY CERTIFY THAT THIS PAPER OR FEE IS BEING  
DEPOSITED WITH THE UNITED STATES POSTAL SERVICE  
"EXPRESS MAIL POST OFFICE TO ADDRESSEE" SERVICE UNDER  
37 C.F.R. 1.10 ON THE DATE INDICATED ABOVE, AND IS  
ADDRESSED TO: BOX PCT, COMMISSIONER FOR PATENTS  
WASHINGTON, D.C. 20231, ATTENTION: DO/US.

KARLY TAMBARA

(TYPED OR PRINTED NAME OR PERSON MAILING PAPER OR FEE)

  
(SIGNATURE OF PERSON MAILING PAPER OR FEE)

This is a request for International Application PCT/US00/05509 to  
enter U.S. national stage under 35 U.S.C. § 371. Commencement of  
national stage processing of this application is expressly  
requested under § 371(f).

International filing date: **March 1, 2000**

Earliest priority date claimed: **March 3, 1999**

Title: **METHOD AND APPARATUS FOR CONTROLLING THE ADSORPTION OF  
A LIQUID SAMPLE THROUGH AN ABSORBENT LAYER**

RECEIVED PROCESSING

01 SEP -5 AM 7:34

Inventor(s): Nelson and Coe  
Docket No.: P-LX 4948  
Page 2

**Basic National fee** under § 1.492(a):

Ch. I search fee was paid to \_\_\_\_\_ USPTO   X   EPO

Ch. II int'l preliminary examination  
fee (IPE fee) was paid to \_\_\_\_\_ USPTO   X   EPO

	Small entity	Other entity
Ch. II IPE fee was paid to the USPTO	___ \$ 345	___ \$ 690
No Ch. II IPE fee was paid to the USPTO, but Ch. I search fee was paid to USPTO	___ \$ 355	___ \$ 710
Neither the IPE fee nor the search fee was paid to the USPTO	___ \$ 500	___ \$1000
Ch. II IPE fee was paid to the USPTO, and the IPER states that all claims meet requirements of novelty, inventive step and industrial applicability	___ \$ 50	___ \$ 100
Ch. I search fee was paid to EPO or JPO	<u>  X  </u> \$ 430	___ \$ 860

**Excess claim fees** under § 1.492(b), (c), (d):

	Number	Number	Rate			Fee	
			Small	Other		Small	Other

09/914684

422 Rec'd PCT/PTO 30 AUG 2001

Inventor(s): Nelson and Coe  
Docket No.: P-LX 4948  
Page 3

**Items that are optional or may be deferred:**

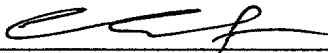
\_\_\_\_ Pages of an executed Declaration for Patent Application  
\_\_\_\_ An executed Power of Attorney for Patent Application by  
Assignee  
\_\_\_\_ Executed Statement Under § 3.73(b)  
\_\_\_\_ Executed assignment and cover sheet  
\_\_\_\_ Information Disclosure Statement  
\_\_\_\_ Paper copy of sequence listing, pages \_\_\_\_ through \_\_\_\_  
\_\_\_\_ Sequence listing in computer readable form  
\_\_\_\_ Statement Under § 1.821(f)  
\_\_\_\_ Translation of the non-English application  
\_\_\_\_ Amendments to the PCT application under Article 19  
\_\_\_\_ Preliminary Amendment  
\_\_\_\_ Also enclosed: \_\_\_\_\_

Please address all future communications to:

Cathryn Campbell  
CAMPBELL & FLORES LLP  
4370 La Jolla Village Drive, 7th Floor  
San Diego, California 92122  
telephone: (858) 535-9001  
facsimile: (858) 535-8949  
**USPTO CUSTOMER NO. 23601**

Respectfully submitted,

Date: August 30, 2001

  
\_\_\_\_\_  
Calvin A. Fan

METHOD AND APPARATUS FOR CONTROLLING THE ADSORPTION OF A LIQUID  
SAMPLE THROUGH AN ABSORBENT LAYER

BACKGROUND OF THE INVENTION

FIELD OF THE INVENTION

The present invention relates to analyzing liquid samples and more specifically to controlling the absorption of a liquid sample by an absorbent layer, thereby reducing the effect of hematocrit.

BACKGROUND INFORMATION

Test strips are widely available for conveniently analyzing liquid samples. Typically, a test strip has one or more layers of absorbent material containing chemical reagents. When the liquid sample is applied to the absorbent layers, the reagents react with the components of interest in the test sample. The resulting reaction can then be measured by a variety of means to yield a measurement of the components in the sample.

For example, it is useful for certain diabetes patients to monitor the concentration of glucose in their blood. A glucose test strip can have an absorbent layer containing reagents that react with glucose present in the blood sample. When a patient applies a blood sample to the absorbent layer, the reagents then react with the glucose in the sample. If the reaction results in a detectable color change -- turning the absorbent layer from colorless to dark blue, for example -- the reaction can then be measured, and the amount of color produced

related to the concentration of glucose in the blood sample.

5 A patient will typically use the test strip  
with a separate device that can measure the chemical  
reaction on the absorbent layer and display the patient's  
blood glucose concentration. One such device uses a  
reflectance meter, which measures reflected light of  
10 specific wavelengths, to monitor the light reflected from  
the surface of the absorbent layer. As the chemical  
reaction in the absorbent layer causes the color change,  
the reflectance meter can monitor the reaction by  
detecting changes in the light reflected from the surface  
of the absorbent layer. For example, as the chemical  
15 reaction proceeds, the reflectance meter can measure an  
increase of blue light reflected from the absorbent layer  
surface. Thus, the reflectance of light from the  
absorbent layer can be used to monitor the chemical  
reaction and thereby determine the glucose concentration  
20 in the blood sample.

However, these reflectance measurements can be  
subject to variability, leading to inconsistent results.  
One factor is the volume of liquid sample applied to the  
25 absorbent layer. Ideally, when the sample is applied to  
the absorbent layer, it should be thoroughly absorbed by  
the layer. In practice, however, excess sample may be  
applied so that the absorbent layer becomes overly  
saturated with the sample. As a result, a layer of  
30 excess sample can collect on the bottom surface of the  
absorbent layer, causing the surface to become shiny.  
This shininess, called *wet-through*, can dramatically  
increase the reflectance of the absorbent layer,  
distorting the measurement of the reaction and providing  
35 misleading information to the patient.

A second variable that can affect the test results is the hematocrit of the patient's blood, which is a measure of the relative amount of red blood cells and plasma in a blood sample. Because the hematocrit of a patient's blood sample can vary, the absorption of the sample by the absorbent layer can vary as well, resulting in hematocrit-dependent measurements of the patient's blood glucose concentration.

Thus, there is a need for controlling the absorption of a liquid sample by an absorbent layer and reducing the effect of hematocrit. The present invention satisfies these needs and provides related advantages as well.

#### SUMMARY OF THE INVENTION

The present invention provides a method for controlling the absorption of a liquid sample through an absorbent layer 2 by (a) providing an air gap 4c defined by the absorbent layer 2, at least one side wall 4d and a translucent window 6; and (b) applying the liquid sample to the absorbent layer on the side opposite to the air gap 2a. As a result, the sample absorption is controlled by preventing the release of air from the air gap 4c.

The present invention also provides an apparatus for performing the method of the invention. The apparatus has an absorbent layer 2, at least one side wall 4d and a translucent window 6, where the layer, walls and window define an air gap 4c.

**BRIEF DESCRIPTION OF THE DRAWINGS**

Figure 1 shows an isometric view of one embodiment of the apparatus (not to scale).

Figure 2 shows a cross-sectional view of one embodiment of the apparatus (not to scale). The plane of the cross-section is indicated in Figure 1.

Figure 3 shows an exploded isometric view of another embodiment of the apparatus including optional elements (not to scale).

For convenience, the elements and features assigned numbers in Figures 1 to 3 are listed below:

- 1: Second layer (optional)
- 2: Absorbent layer, with application surface **2a** and opposite viewing surface **2b**.
- 3: Adhesive layer with hole **3c** and inner surface **3d**
- 4: Handle, with hole **4c** and inner surface **4d**
- 5: Adhesive layer with hole **5c** and inner surface **5d**
- 6: Translucent window with surface **6a**.
- 7: Generalized line of sight

Figure 4 compares the relative volume-dependence of test strip Model A (with air gap) and Model B (without air gap).

Figure 5 compares the relative hematocrit-dependence of test strip Models A and B.

DETAILED DESCRIPTION OF THE INVENTION

5 The present invention provides a method and apparatus for controlling the absorption of a liquid sample by an absorbent layer. When a liquid sample is applied to the application surface **2a** of the absorbent layer **2**, the sample is absorbed. As shown in the embodiment of Figure 2, an air gap **4c** is provided, defined by the viewing surface **2b** on the opposite side of  
10 the absorbent layer **2**, at least one side wall **4d** and a surface of a translucent window **6a**. The "air gap" thus defined is an air-tight chamber with ambient air pressure.

15 Absorption of the liquid sample causes a slight increase in pressure within the air gap compared with the ambient pressure. This pressure increase can be explained by the decrease in effective volume of the air gap as the liquid absorbed by the layer displaces air  
20 within the layer. Because the air gap lacks an exit for the displaced air to escape, the air gap effectively prevents further sample from being absorbed by the absorbent layer.

25 As a result of the air gap, excess sample is not absorbed by the absorbent layer, but may pool on the application surface **2a** or be absorbed by an optional second layer **1**. Otherwise, a layer of excess sample could form on the viewing surface of the absorbent layer  
30 **2b**, an undesirable result called *wet-through*. Thus, absorption of excess liquid sample is controlled by providing an air gap.



"Liquid samples" that can be used with the invention encompass any fluid containing an analyte to be measured, for example blood, serum or plasma. The term also encompasses other "human body fluids" such as sweat, tears, saliva, semen, cerebrospinal fluid, sputum, urine and cervical mucus or swabbings. The term further encompasses food, environmental or industrial samples, depending on the desired application of the article, as long as they are liquid and contain an analyte for measurement.

The liquid sample can be analyzed for specific "analytes" of interest, which are any substances to be detected or quantitated in terms of concentration. For example, the analyte can be glucose, fructose, or other sugars, cholesterol, ketones, lipids, uric acid or specific amino acids such as phenylalanine. The analyte can also be proteins, for example enzymes such as amylase, creatine kinase or alanine aminotransferase. Furthermore, the analyte can be glycated proteins, for example serum or plasma glycated protein as measured by fructosamine, or red blood cell glycated protein as measured by glycated hemoglobin, in particular Hb<sub>A1c</sub>. Other analytes are described in U.S. Patent No. 5,597,532, incorporated herein by reference.

The "absorbent layer" can be any material that is permeable to gas when dry and can absorb liquid, but is relatively less permeable to gas when saturated or partially saturated with liquid. A particular absorbent layer is BIODYNE A 0.65  $\mu\text{m}$  pore size nylon membrane (Pall Corp.; East Hills, New York). The absorbent layer can contain a reagent that indicates the presence of an analyte such as glucose or fructosamine. Representative absorbent layers are described in U.S. Patent No.

5,470,752, U.S. Patent No. 5,597,532 and U.S. Patent No. 5,695,949, each incorporated herein by reference.

5 A particularly useful absorbent layer contains  
a reagent that reacts with glucose in the liquid sample,  
for example a glucose oxidase/horseradish peroxidase  
system (Toyobo Inc.; Tokyo, Japan). Another useful  
system for reacting with glucose is N-ethyl-N-2-hydroxy-  
10 3-sulfopropyl-3,5-dimethylaniline (MAOS) (Dojindo  
Laboratories; Kumamoto, Japan) and N-ethyl-N-(2-hydroxy-  
3-sulfopropyl)-*m*-toluidine (TOOS). Other reagents  
include the combination of 4-aminoantipyrene and  
chromotropic acid (AAP-CTA) and the combination of 3-  
15 methyl-2-benzothiazoline hydrazone hydrochloride (MBTH)  
and either 3-dimethylaminobenzoic acid (DMAB) or 8-anilo-  
1-naphthalenesulfonate (ANS).

20 The absorbent layer can be attached to a handle  
4 so the user to hold the test strip without touching the  
absorbent layer. The handle contains a hole 4c, whose  
inner walls 4d partially define the air gap. For  
example, Figure 3 shows that the side wall 4d is the  
inner surface of a hole 4c. Although hole 4c is circular  
in Figure 3, it can also be of any shape so that there  
25 can be two or more distinct side walls forming the air  
gap.

30 The handle 4 can be attached to the absorbent  
layer 2 by any means for adhering two layers together so  
long as the resulting air gap is secure against the  
escape of air and does not occlude the viewing surface of  
the absorbent layer 2b along the line of sight 7. For  
example, the means for adhering can be acrylic-, rubber-  
or silicone-based adhesives. A particularly useful

acrylic-based adhesive layer is FAS-TAPE 8311 double-coated acrylic-based adhesive (Avery-Dennison, Inc.; Pasadena, California). Other adhesives include 3M 444 or 3M 415 double-coated adhesives (3M; Minneapolis, Minnesota). Means for adhering the sintered polymer to the solid can also include PVC plastic pipe cement, epoxy, heat staking, clamping, bolting, nailing, compression fitting and immobilization by vacuum.

The test strip also has a translucent window **6**, which partially defines the air gap **4c** by one of its surfaces **6a**. The "translucent window" should allow light to travel substantially along line of sight **7** to pass through the window **6** and reach the viewing surface **2b** and be reflected back through window **6** so that the reflected light can be detected.

Because the liquid sample may be warmer or colder than the ambient temperature may form on a surface of the window **6**, interfering with light along the line of sight. Accordingly, the window may be treated to be "non-fogging" so that temperature differences in the window do not result in condensation of moisture from the ambient atmosphere. The window **6** can be attached to the handle **4** by any of the means for adhering two layers discussed above.

Thus, as shown in Figure 3, an adhesive layer **3** can be used to attach the absorbent layer **2** to the handle **4**, and another adhesive layer **5** can be used to attach the handle **4** to the window **6**. In such cases, the adhesive layers **3** and **5** should have holes **3c** and **5c** so that they do not interfere with line of sight **7**. Furthermore, the air gap will then be defined by the viewing surface of

the absorbent layer **2b**, by the inner side walls of the adhesive layer **3d**, of the handle **4d** and of the second adhesive layer **5d**, and by the surface of the window **6a**.

5 Additional layers can be added to the apparatus, for example a second layer **1** for separating a whole blood sample and allowing blood plasma to reach the application surface of absorbent layer **2a**. Such layers are well known in the art and are exemplified by the  
10 whole blood separation layers in U.S. Patent No. 5,725,774, which is incorporated by reference.

### EXAMPLES

#### **I. Construction of test strip with air gap**

15 To compare the performance of test strips with and without the air gap feature, three models of test strips were assembled: Model A with the air gap and  
20 Models B and C without an air gap. Each of the models had a solid polyester handle **4** and an absorbent layer **2**, which was BIODYNE A 0.65  $\mu\text{m}$  pore size nylon membrane (Pall Corp.; East Hills, New York). The absorbent layer  
25 was impregnated with a glucose oxidase/horseradish peroxidase system (Toyobo Inc.; Tokyo, Japan) and MAOS (N-ethyl-N-2-hydroxy-3-sulfopropyl-3,5-dimethylaniline, sodium salt, monohydrate) (Dojindo Laboratories; Kumamoto, Japan). The handle **4** and absorbent layer **2**  
30 were attached with an adhesive layer **3**, which was FAS-TAPE 8311 double-coated acrylic-based adhesive (Avery-Dennison, Inc.; Pasadena, California). These common features were modified in the three models as follows.

Model A, which featured the air gap, also had a translucent window 6 of MYLAR D 4 mil-thick transparent polyester film (Dupont & Co.; Wilmington, Delaware). The film was treated by dipping in PERFECT VIEW non-aerosol anti-fog lens cleaner (Tyr Sport Inc.; Huntington Beach, California). The film was attached to the handle 4 by an adhesive layer 5, which was the same as adhesive layer 3 above. A second layer 1 was T667 or 6664 spunbonded white polyester fabric (Reemay, Inc.; Old Hickory, Tennessee). The second layer was treated with between 0.0001% and 0.1% PLURONIC polyoxypropylene polyoxyethylene block copolymer (Pragmatics Inc.; Oak Ridge, Tennessee), 8% mannitol, and 0.15% hexadimethrin, all in a 0.85% NaCl solution.

Model B had a second layer 1 of hydrophillic 0.0635 cm thick POREX XM-1342 sintered high density polyethylene (HDPE) treated as described for second layer 1 in Model A. The layer was further treated as described in U.S. Patent Application Ser. No. 09/006,787, filed January 14, 1998.

Model C had a second layer 1 of T667 or 6664 spunbonded white polyester fabric (Reemay, Inc.; Old Hickory, Tennessee). The second layer was treated as described for second layer 1 in Model A.

## II. Preparation of test samples and measurement methods

Whole blood samples, treated with tripotassium ethylenediaminetetraacetate (EDTA) as an anticoagulant, were prepared by allowing the samples to metabolize to a value less than 50 mg/dL, then spiking the sample with a

concentrated glucose solution. The final glucose concentration of the sample was verified by a YSI Stat-2300 Glucose Analyzer (Yellow Springs Instruments Inc., Yellow Springs, Ohio).

5 The sample was then applied to a test strip when inserted into a device containing a reflectance meter. A light-emitting diode (LED) in the device directed light having a wavelength of 635 nm to the viewing surface of the absorbent layer **2b** essentially along line of sight **7**. The reflectance of the viewing surface **2b** was measured by the reflectance meter over time using a silicon photodiode, which generated an analog signal. The signal was then processed by a transconductance amplifier, a synchronous detector, an analog-to-digital converter and a microprocessor. Automated processing and analysis of such detector signals is well known in the field of medical devices (see, for example, U.S. Patent 5,597,532). The microprocessor then displayed the calculated values for the concentration of glucose based on a standard curve using samples having known glucose concentrations.

### 25 **III. Improved measurement consistency of from using air gap**

30 The following example shows that test strips featuring an air gap provide more consistent measurements than models without an air gap.

Blood samples with an adjusted hematocrit of 40% were prepared at five concentrations of glucose: about 50, 100, 200, 350 and 500 mg/dL. The

concentrations were later verified by the YSI Stat-2300 Glucose Analyzer. Samples of 15  $\mu$ L were applied to 16 strips of each of the three models and measured using the device described in Example II. The results were as follows in terms of the percent coefficient of variation (%CV = standard deviation / mean):

Glucose mg/dL (by YSI)	Model A %CV	Model B %CV	Model C %CV
60	2.1	3.6	4.3
106	2.9	3.2	2.2
197	4.0	10.3	4.2
351	2.3	6.6	6.6
520	3.8	7.4	9.8
average %CV:	3.0	6.2	5.4

These results show that Model A, which features the air gap, has a significantly less variability than Models B and C, which do not feature an air gap, resulting in more consistent measurements.

#### IV. Reduced volume-dependency from using air gap

As discussed above, the measured glucose concentration may vary, depending on the volume of the sample applied to the strip, because of wet-through. The following example shows that the measurements from test strips with an air gap are less subject to variation due to changes in the volume of the sample.

Blood samples were prepared at about 100, 300 and 500 mg/dL as described in Example III. Samples of

3.5, 4, 5, 10, 15, 20, 30 and 40  $\mu$ L of each concentration were applied to 4 strips each of models A and B, and measured using the device described in Example II.

5           The results are shown in Figure 4, which show the average measured glucose concentrations (y-axis) using models A (three sets of solid lines) and B (three sets of dotted lines) for varying sample volumes (x-axis) and varying actual glucose concentrations (upper, middle and lower pairs of solid and dotted lines). It is  
10           apparent that measured glucose concentrations for Model A, with the air gap, is more consistent across a range of sample volumes from 4  $\mu$ l to 40  $\mu$ l. In contrast, the measurements from Model B are only somewhat consistent  
15           between 10  $\mu$ l and 40  $\mu$ l.

          This shows that the measured concentration using Model A, which has an air gap, is less likely than Model B to be affected by the volume of the sample.

#### 20           **V. Improved hematocrit-independence from using air gap**

          Measurements of glucose concentration can also vary depending on the hematocrit, which is a measure of  
25           the relative amounts of red blood cells and plasma in a blood sample. The following example shows that the results from test strips with an air gap are less likely to be affected by the hematocrit of the blood sample than test strips without an air gap.

30           Blood samples were prepared at about 100, 200 and 400 mg/dL as described in Example III with hematocrits of 0 (plasma), 20, 30, 40, 50, 60 and 80%, where 80% represents the hematocrit of a sample when it  
35           is spun at 5000 rpm for 30 minutes and all plasma is



removed. Sample volumes of 15  $\mu$ l were applied to each of 8 strips of Models A and B each, using the device described in Example II.

5           These results, as shown in Figure 5, show the average measured glucose concentrations (y-axis) using models A (three sets of solid lines) and B (three sets of  
10           dotted lines) for varying sample hematocrit values (x-axis) and varying actual glucose concentrations (upper, middle and lower pairs of solid and dotted lines). It is apparent that Model A yields relatively consistent glucose measurements over the range of hematocrit values. In contrast, Model B can yield misleadingly low  
15           measurements as the hematocrit increases, especially when the sample contains high concentrations of glucose. Thus, the measurements using Model A, which features the air gap, are less hematocrit-dependent than Model B, which lacks an air gap.

20           Although the present invention has been described by the disclosed embodiments, those skilled in the art will readily appreciate that the specific examples are provided to illustrate, not to limit, the invention. It should be understood that various  
25           modifications can be made without departing from the spirit of the invention. Accordingly, the invention is limited only by the following claims.

We claim:

1. A method for controlling the absorption of  
a liquid sample through an absorbent layer, comprising  
5 the steps of

(a) providing an air gap defined by an  
absorbent layer, at least one side wall  
and a translucent window; and

(b) applying a liquid sample to the absorbent  
layer on the side opposite to the air gap;

whereby sample absorption is controlled by  
preventing the release of air from the air gap.

2. The method of claim 1, wherein the sample  
is a human body fluid.

3. The method of claim 2, wherein the fluid is  
a blood sample.

4. An apparatus comprising an absorbent layer,  
at least one side wall and a translucent window, wherein  
the layer, walls and window define an air gap.

5. The apparatus of claim 4, wherein the  
window is non-fogging.

6. The apparatus of claim 4, wherein the  
absorbent layer contains a reagent that indicates the  
presence of an analyte.

7. The apparatus of claim 4, further comprising a second layer in contact with the absorbent layer.

WO 00/52468 PCT/US00/05509

1/4

Fig. 1

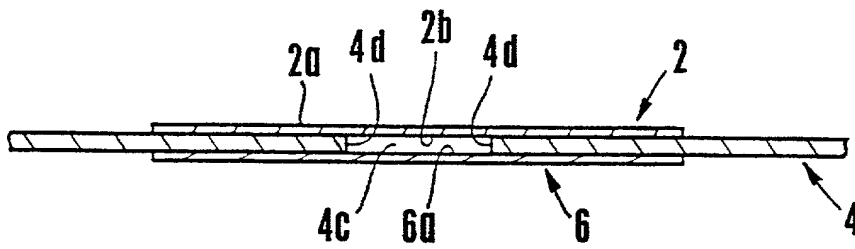
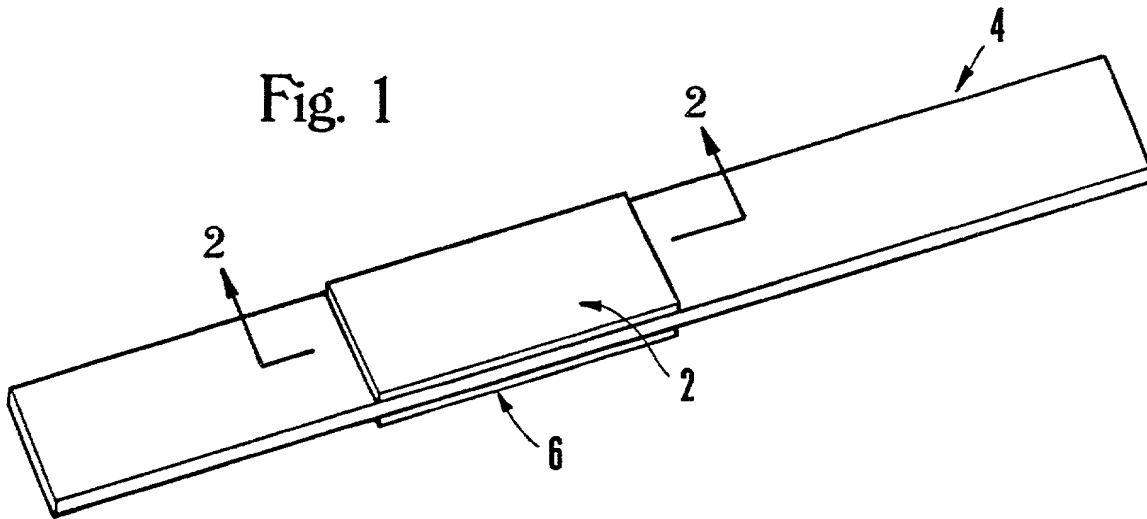


Fig. 2

2/4

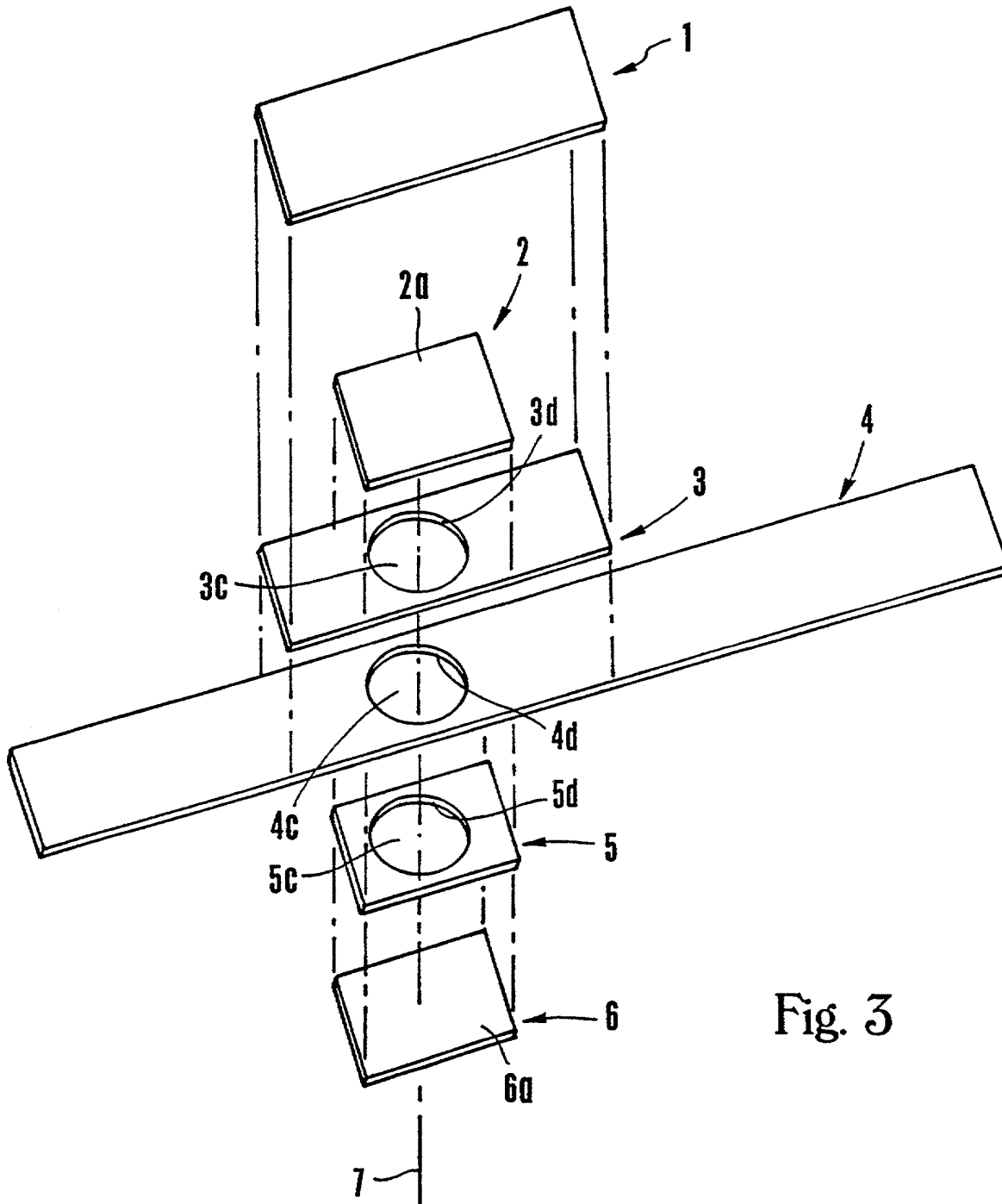


Fig. 3

Fig. 4

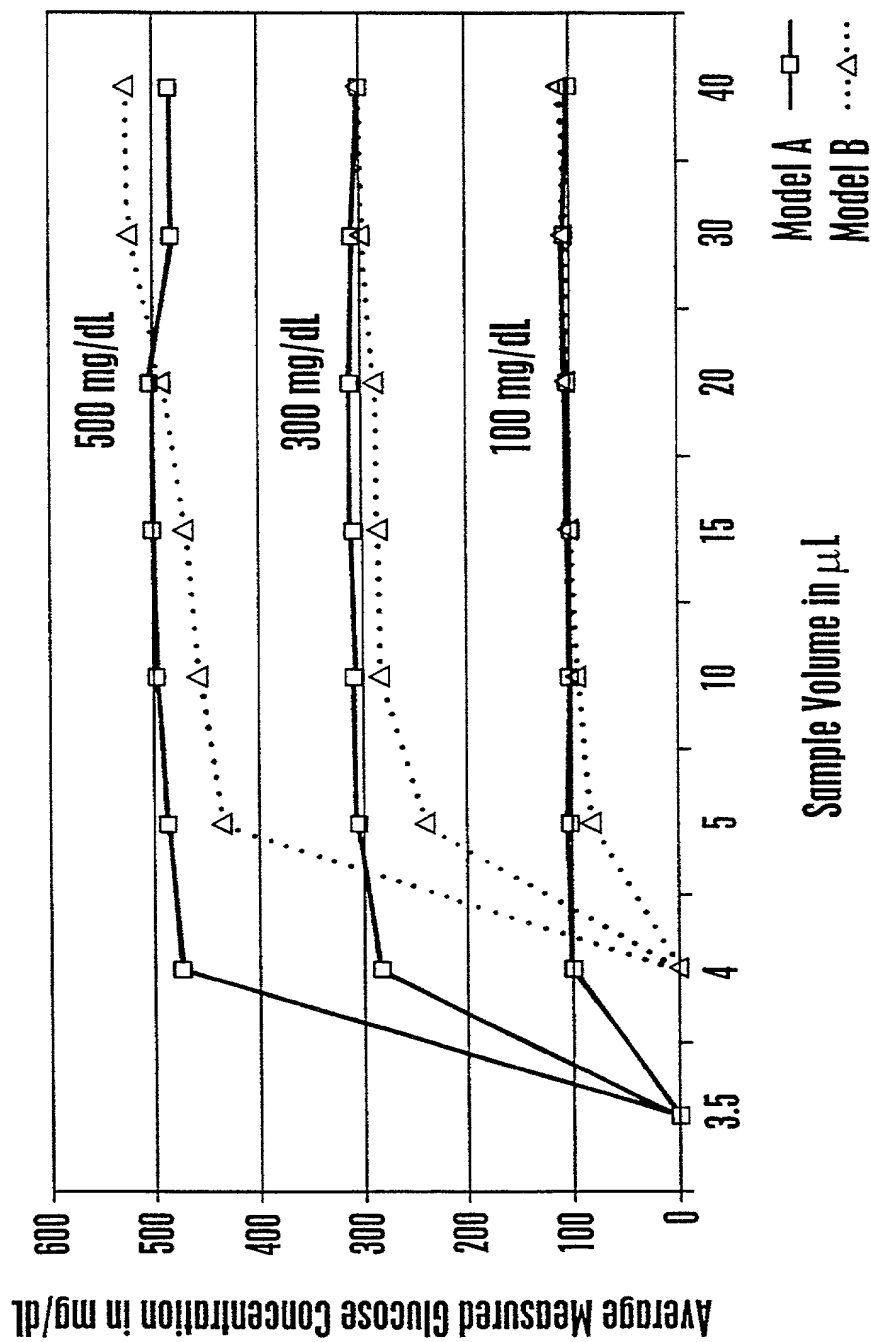
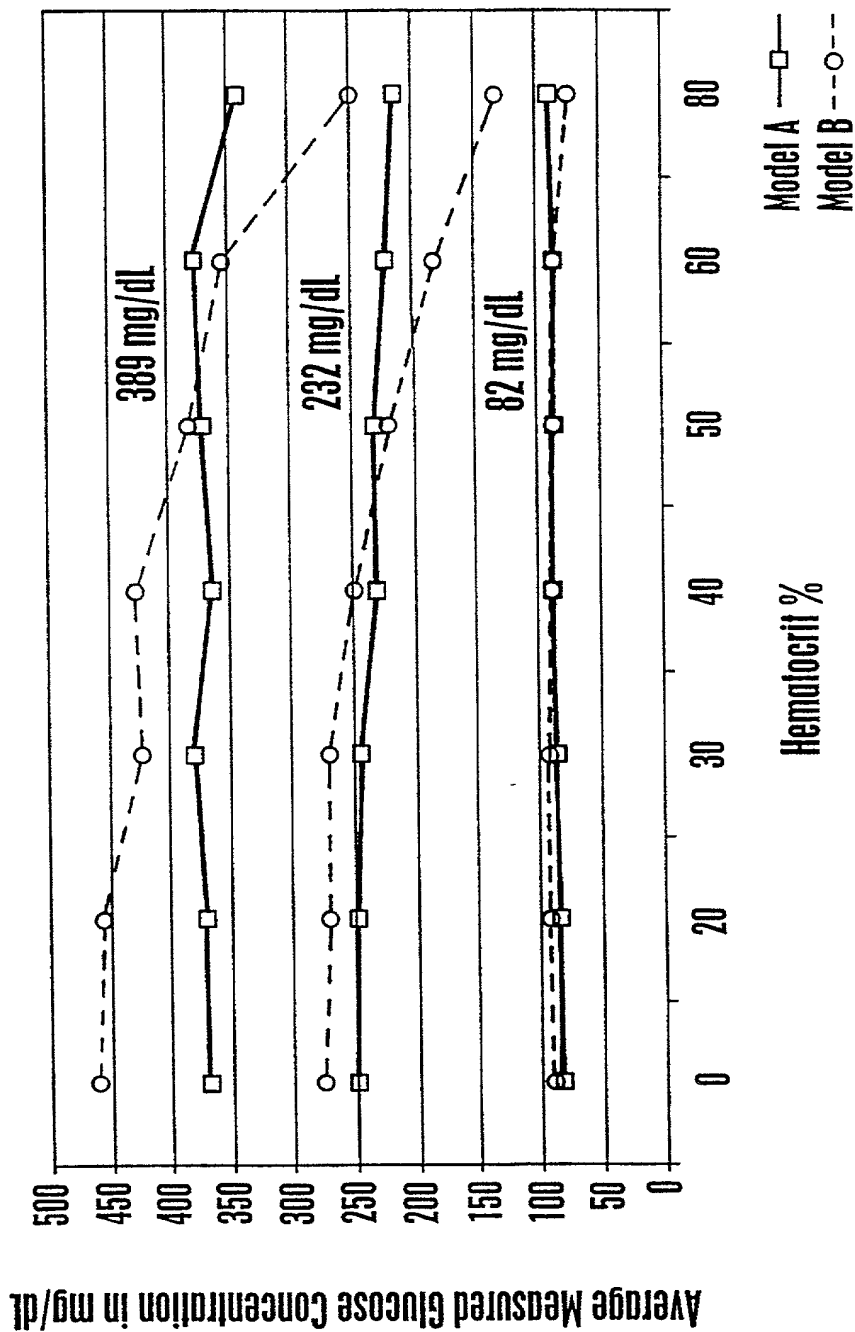


Fig. 5



POWER OF ATTORNEY

Assignee **LXN Corporation**

is the owner of the entire right, title and interest of the following U.S. patent application identified below and any subsequently filed divisional, continuation, continuation-in-part or reissue applications claiming priority thereto.

Title: **METHOD AND APPARATUS FOR CONTROLLING THE ADSORPTION OF A LIQUID SAMPLE THROUGH AN ABSORBENT LAYER**

International Patent Application No. **PCT/US00/05509**

International filing date: **March 1, 2000**

Claiming priority to prior **United States** application

Serial No. **09/261,707**

Filing (priority) date: **March 3, 1999**

Entry into U.S. national stage as Serial No. **09/914,684**

U.S. National Stage entry date: **August 30, 2001**

U.S. Applicants/Inventors: **Eric M. Nelson and Matthew A. Coe**

Campbell & Flores Attorney Docket No. **P-LX 4948**

The Assignee hereby appoints the following attorneys to prosecute these applications and to transact all related business in the United States Patent and Trademark Office:

CATHRYN CAMPBELL,	Registration No. <u>31,815</u> ;
DAVID A. GAY,	Registration No. <u>39,200</u> ;
CALVIN A. FAN,	Registration No. <u>38,444</u> ;
ANDREA L. GASHLER,	Registration No. <u>41,029</u> ;
JAMES J. WONG,	Registration No. <u>34,949</u> ;
DEBORAH L. CADENA,	Registration No. <u>44,048</u> ;
MELANIE K. WEBSTER,	Registration No. <u>45,201</u> ;
ASTRID R. SPAIN,	Registration No. <u>47,956</u> ;
MARGARET M. PARR,	Registration No. <u>48,111</u> ; and
KIMBERLY J. PRIOR,	Registration No. <u>41,483</u> .

10



Inventors: Nelson and Coe  
Serial No. 09/914,684  
Filed: August 30, 2001  
Page 2

Please direct all telephone calls to Cathryn Campbell at  
(858) 535-9001 and address all correspondence to

CATHRYN CAMPBELL  
CAMPBELL & FLORES LLP  
4370 La Jolla Village Drive  
7th Floor  
San Diego, California 92122  
USPTO CUSTOMER NO. 23601

The undersigned is empowered to sign this statement on behalf of  
the assignee.

Date: December 3, 2001

Signature: Sandra F. Selvaggi

Name: Sandra F. Selvaggi

Title: Sr. Director, Corporate  
and Regulatory  
Affairs

LXN Corporation  
6325 Lusk Blvd.  
San Diego, California 92121

20011203 14:58

DECLARATION

Title: METHOD AND APPARATUS FOR CONTROLLING THE ADSORPTION  
OF A LIQUID SAMPLE THROUGH AN ABSORBENT LAYER

International Patent Application No. PCT/US00/05509

International filing date: March 1, 2000

Claiming priority to prior United States application

Serial No. 09/261,707

Filing (priority) date: March 3, 1999

Entry into U.S. national stage as Serial No. 09/914,684

U.S. National Stage entry date: August 30, 2001

U.S. Applicants/Inventors: Eric M. Nelson and Matthew A. Coe

Campbell & Flores Attorney Docket No. P-LX 4948

I believe that I am an original and first inventor of the  
subject matter that is claimed and for which a patent is sought  
in the application identified above.

I hereby state that I have reviewed and understand the contents  
of the application identified above, including the specification  
and claims.

I acknowledge the duty to disclose to the U.S. Patent and  
Trademark Office all information known to myself to be material  
to patentability as defined in Title 37, Code of Federal  
Regulations, Sec. 1.56.

Under Sec. 1.56, information is material to patentability when  
it is not cumulative to information already of record or being  
made of record in the application, and (1) It establishes, by  
itself or in combination with other information, a prima facie

Inventors: Nelson and Coe  
Serial No. 09/914,684  
Filed: August 30, 2001  
Page 2

case of unpatentability of a claim; or (2) It refutes, or is inconsistent with, a position the applicant takes in: (a) Opposing an argument of unpatentability relied on by the U.S. Patent and Trademark Office, or (b) Asserting an argument of patentability.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

My citizenship, residence and mailing address are correctly stated below my name:

Full name of first inventor: Eric M. Nelson

Citizenship: USA

Residence: ~~San Clemente, California~~ Binningen, Switzerland

Mailing Address: ~~2174 Via Teca, San Clemente, CA 92673~~

Rottmannsbodenstrasse 122 B CH-4102 Binningen, Switzerland

Signature: Eric M. Nelson Date: 13-Nov-01

Inventors: Nelson and Coe

Serial No. 09/914,684

Filed: August 30, 2001

Page 3

2-20

Full name of second inventor: Matthew A. Coe

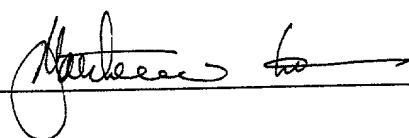
Citizenship: USA

Residence: La Mesa, California

CA

Mailing Address: ~~5014 Williams Ave.~~, La Mesa, CA 91941

4353 Dale Ave Me 11.13.01

Signature:  Date: 11.13.01

2001-08-30 14:44:50